Age-Related Peculiarities of Heart Rate in Intact and Sympathectomized Rats Injected with Atropine

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 128, No. 12, pp. 627-629, December, 1999
Original article submitted April 22, 1999

Atropine induced various changes in the heart rate in intact rats of various ages. In sympathectomized animals, changes in heart rate variability were less pronounced. Atropine blocked the inhibition of cardiac activity induced by electrical stimulation of the vagus nerve.

Key Words: *rat; heart rate; sympathectomy; atropine; vagus nerve*

Vagotomy sharply increases heart rate (HR) in dogs and cats [7]. Atropine, a nonspecific muscarinic receptor (MR) blocker, induces similar effects [2,8, 9,11]. Experimental data suggest that the vagus nerves induce tonic effects on the chronotropic heart function. At the same time, some authors believe that the vagus nerves induce no inhibitory effects [6,9], and acceleration of HR after vagotomy and atropine administration is due to excitation of the sympathoadrenal system. Low doses of atropine cause bradycardia, but not tachycardia [10,11]. HR reactions to vagotomy and atropine considerably differ in various animal species [8]; postvagotomy tachycardia is least pronounced in small rodents [5]. Therefore, the effects of atropine on HR in rats are of considerable interest.

The population of MR is heterogeneous [12]. The ratio between various MR subtypes changes with age probably due to the development of sympathetic cardiac innervation during the postnatal ontogeny [13, 14]. Our previous experiments demonstrated age-related peculiarities of HR response to uni- or bilateral vagotomy in intact and sympathectomized animals [3]. Here we studied the role of MR in the development and regulation of HR in intact and sympathectomized rats during the postnatal ontogeny.

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MATERIALS AND METHODS

Experiments were performed on 58 outbred albino rats aging 4, 6, 8, and 20 weeks. Sympathectomy was induced by administration of 10 ml/kg guanethidine sulfate to 36 newborn rats for 28 days. The rats were intraperitoneally narcotized with 25% urethane in a dose of 800 mg/kg. Atropine sulfate in a dose of 0.6 mg/kg was injected into the right femoral vein.

Stimulation of the right and left vagus nerves (individual parameters for each animal) was performed before and after the injection of atropine at 15-min intervals using an ESL-2 device. Electrocardiogram (ECG) was visually controlled with an S1-83 oscillograph [1]. We analyzed 8 of 13 parameters of R-R intervals [4] reflecting activity of the major regulatory mechanisms: mean cardiac interval (X_m), mode (M), mode amplitude (MA), variational range (ΔX), mean deviation (δ), strain index, and HR.

The results were analyzed by Student's *t* test.

RESULTS

Electrical stimulation of the vagus nerves reduced HR in intact and sympathectomized rats (Fig. 1). In intact animals, the inhibition of cardiac activity induced by stimulation of the right vagus nerve increased with age. Stimulation of the right and left vagus nerves considerably reduced HR in sympathectomized rats of all groups. The dynamics of parameters of variational

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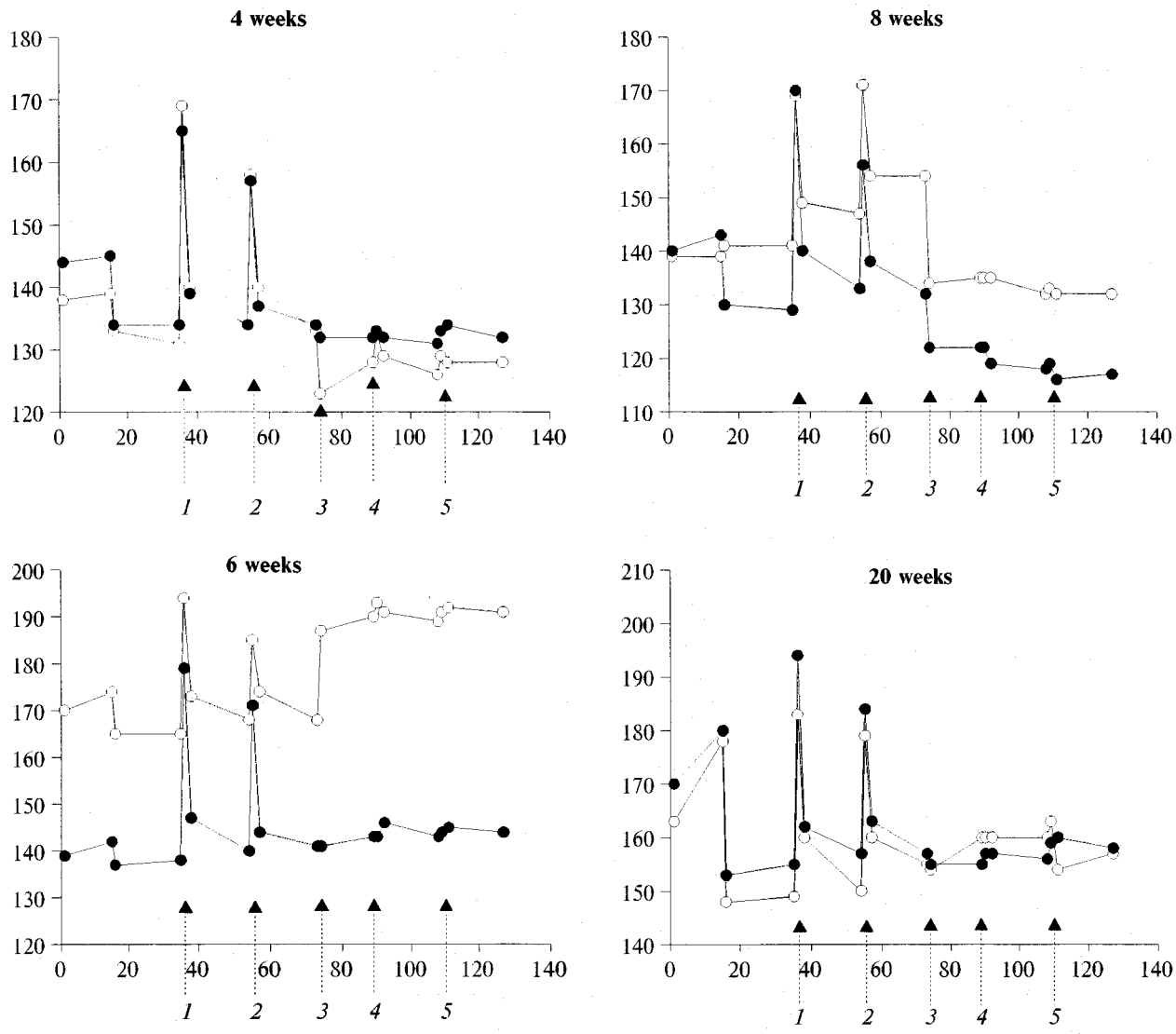

Fig. 1. Mean cardiac intervals in intact (dotted line) and sympathectomized (solid line) rats of various ages after stimulation of the right (*1*, *4*) or left vagus nerves (*2*, *5*) and atropine injection (*3*). Abscissa: time, min; ordinate: mean cardiac interval, msec.

pulsogram suggested that stimulation of the vagus nerves activated the parasympathetic regulation of cardiac activity.

Atropine induced different effects on HR variability in intact and sympathectomized rats of various ages (Fig. 1). In intact rats, atropine accelerated HR (by 8%) in 4-week-old and decreased it in 6-week-old animals. The increase in X_m by 11% ($p<0.05$) was accompanied by an increase of δ and ΔX reflecting cardiac automaticity. The administration of atropine to 8-week-old animals increased HR ($p<0.001$) and decreased X_m by 13%. In adult intact rats, atropine slightly increased HR (by 1%). The dynamics of other parameters of variational pulsogram after injection of atropine also had age-related peculiarities. The increase in ΔX and MA after the injection of atropine to 6-week-old animals is of particular interest, because these parameters of HR variability reflect activity of the sympathetic and parasympathetic nervous systems and usually undergo opposite changes.

Sympathectomized and intact animals displayed different reactions to atropine (Fig. 1). MR blockade in 4- and 20-week-old sympathectomized animals led to a minor acceleration of HR. Atropine did not change X_m in 6-week-old sympathectomized rats, but accelerated HR ($p<0.01$) and decrease X_m (by 8%) in 8-week-old sympathectomized animals. Changes in the dynamics of variational pulsogram in sympathectomized rats injected with atropine were similar, but less pronounced than in intact animals.

In all groups of intact and sympathectomized rats, atropine abolished HR inhibition but did not prevent changes in other parameters of variational pulsogram induced by electrical stimulation of the vagus nerves.

Comparative analysis revealed marked age-related peculiarities of heart rate reactions to MR blockade with atropine, which induced different and even opposite chronotropic effects: tachycardia in 8-week-old and bradycardia in 6-week-old rats (Fig. 1).

Atropine-induced changes in HR variability in sympathectomized rats were less pronounced than in intact animals. These findings suggest that sympathetic neurons probably modulate activities of parasympathetic postganglionic neurons in intracardiac ganglia, which release acetylcholine that binds MR on myocardiocytes.

Considerable age-related peculiarities of HR response in 6- and 8-week-old rats (prepubertal and pubertal periods, respectively) are probably due to the reconstruction of the hypothalamo-pituitary and endocrine systems and the development of sympathetic innervation of the heart during sexual maturation.

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